

# Preparing Electronic Drug Establishment Registration and Drug Listing Submissions in SPL Format

## **SPL R4 101**

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# Structured Product Labeling Overview

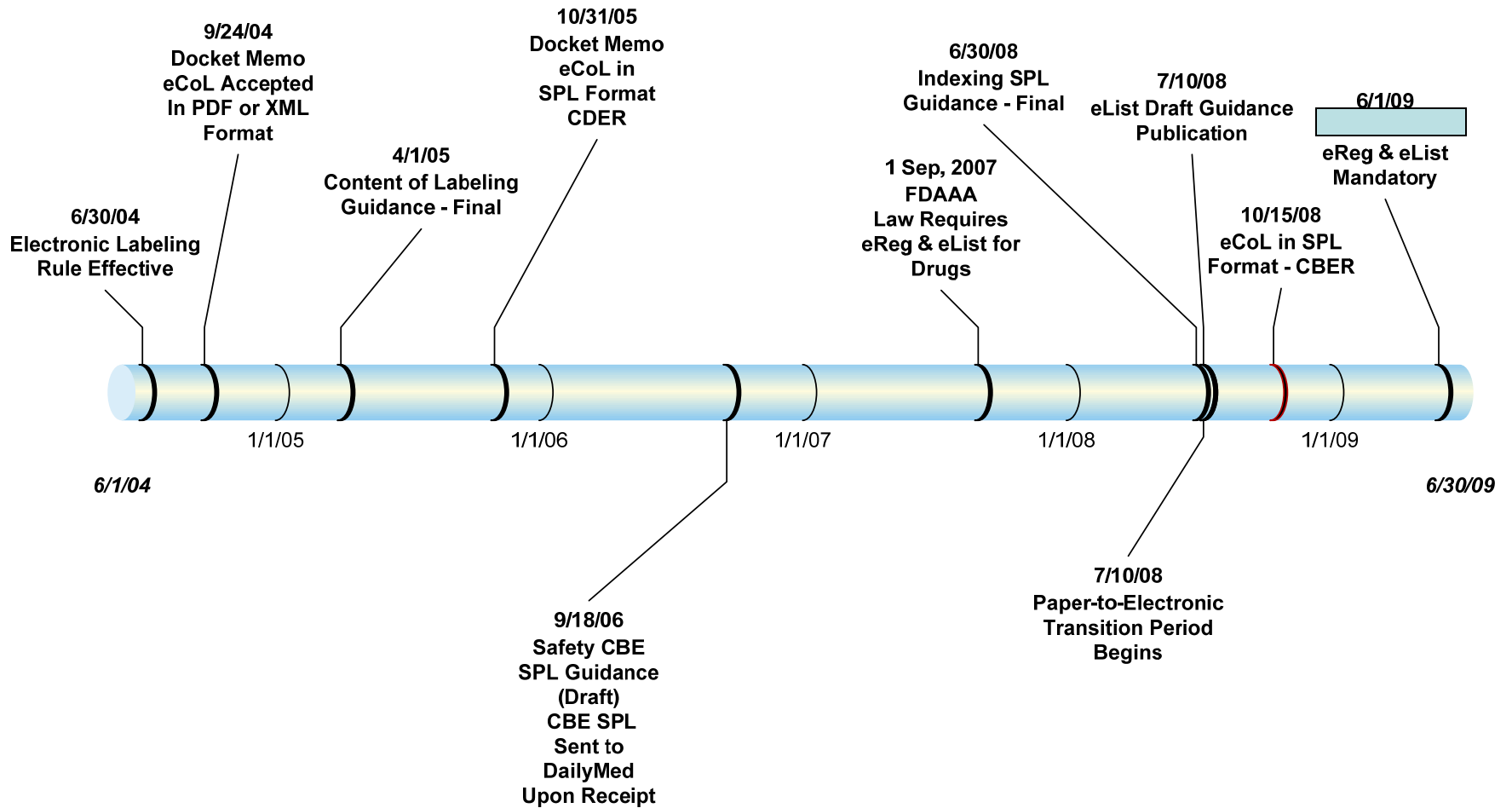
# SPL Standard

- The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product information.
- American National Standards Institute (ANSI) accredited (SPL Release 4) – March 2009
- SPL is created using **EX**tensible **M**arkup **L**anguage

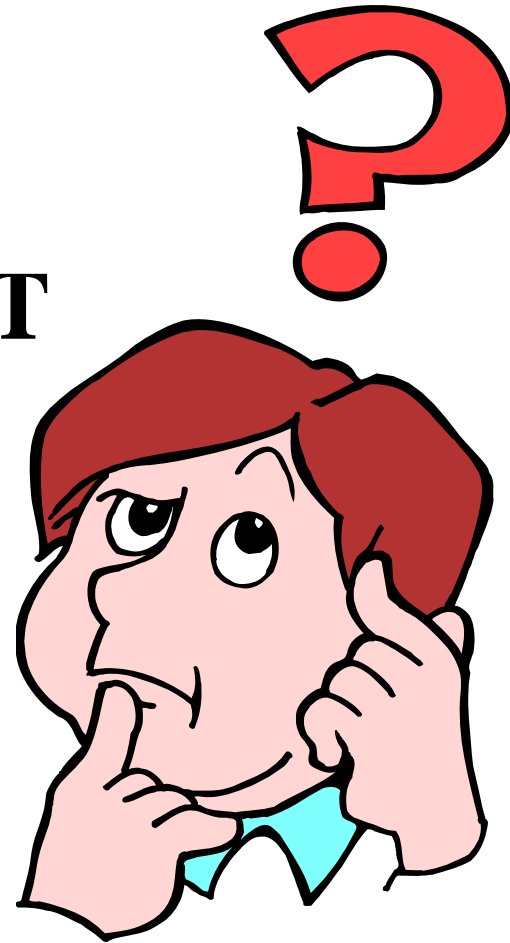
# XML & XSL Stylesheet

- XML – **EX**tensible **M**arkup **L**anguage
  - Relatively human-legible
  - Machine readable
  - Tags (elements) permit search of key information
- XML Documents – created via Notepad, Word Pad, XML validation tools, Xforms, etc...
- XSL Stylesheet – transforms the XML data to be viewed via web browser or printed documents

## IMPLEMENTATION OF STRUCTURED PRODUCT LABELING AT FDA



**WHY CHANGE  
THE DRUG LISTING  
AND ESTABLISHMENT  
REGISTRATION  
PROCESS THAT HAS  
WORKED FOR  
DECADES ????**



- Eliminate duplicative and redundant data entry
- Eliminate paper submissions
- Automate processing of data in a submission type in electronic format in a manner that FDA can adequately process, review, and archive.

# Transition from Paper to Electronic Drug Establishment Registration & Drug Listing

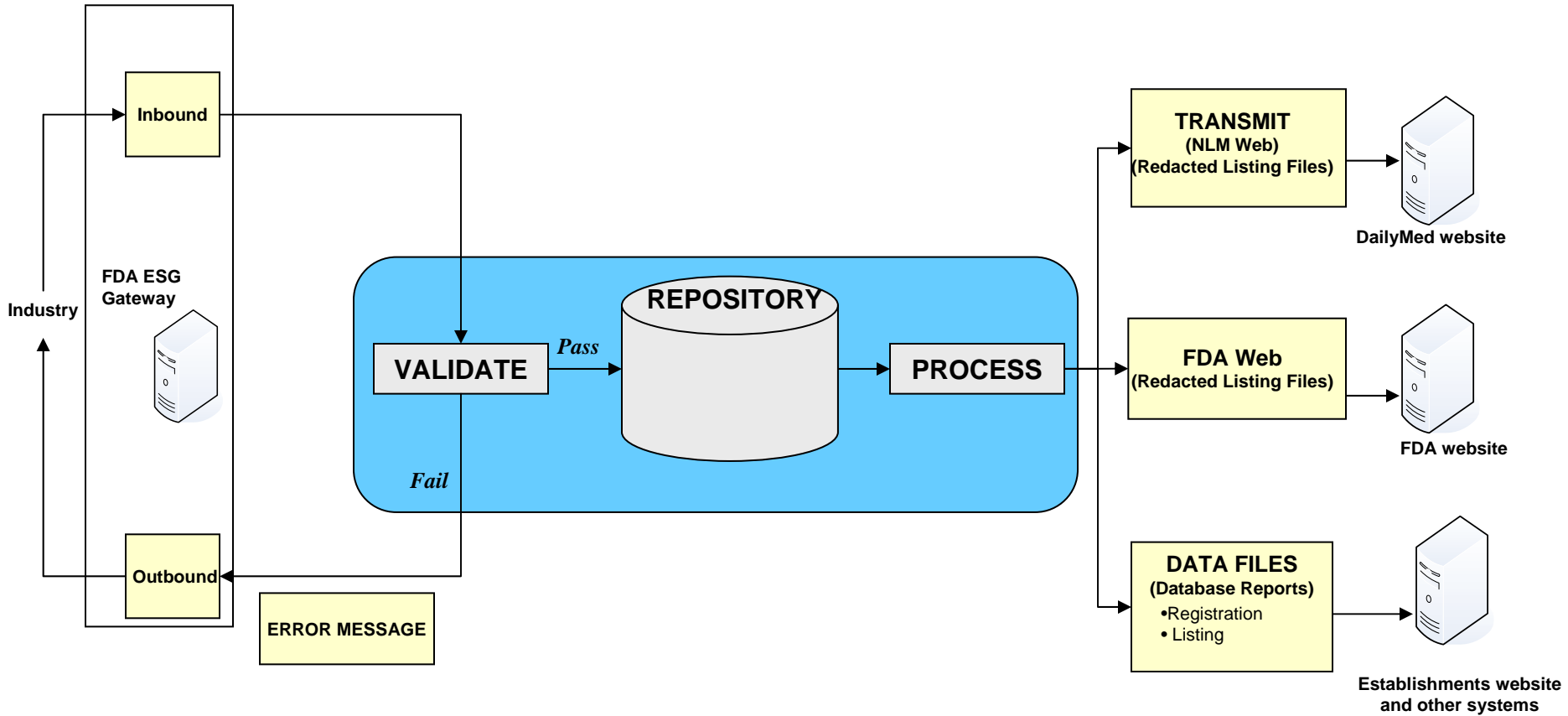
- Changes in FD&C Act require electronic registration of drug establishments and listing of human prescription drugs, OTC, animal drug, biologic products – September 2007
- Final guidance document for electronic drug establishment registration and listing – May 2009
- FDA is adopting the use of extensible markup language (XML) files in SPL format as the standard format for the exchange of drug establishment registration and drug listing information.



# Benefits of Electronic Registration and Listing

- Electronic registration and listing process is more efficient and effective for industry and the Agency
- Accurate, up-to-date inventory of marketed drugs
- Eliminates data entry errors
- Eliminates the use of paper forms for listing and registration
- 24-hour submission window – FDA Gateway
- Reduces the amount of time for FDA to receive and process your information.
- Well formed and properly created SPL files can be processed in minutes
- Receive submission feedback in timely manner
- OTC drug product listing data is included in database

# eLIST



# SPL Training Documents

- **Use** these most recent version of these source documents when authoring your SPL:
  - SPL Validation Procedures
  - SPL Step-by-Step instructions document
  - Appropriate regulatory guidance documents
  - Appropriate labeling and listing regulations
  - SPL Training eBooks (<http://spl-work-group.wikispaces.com/SPL+eBooks+--+Graphic+Guides>)
  - SPL Pathways Training eBooks (<http://spl-work-group.wikispaces.com/SPL+Pathways+Training>)
  - Most SPL-related regulatory guidance and technical documents are available on FDA Data Standards Council website – SPL Labeling Resources web page  
<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

NDC Labeler Code SPL

# NDC Labeler Codes

- Labeler code already assigned?
  - Submit labeler code SPL file to add your labeler code to our electronic system
  - Submit only labeler codes to be utilized in NDCs which will be included in future drug listing SPL documents

# NDC Labeler Codes

- Request for new labeler code
  - Only if you need a new labeler code to generate NDCs to distribute products
  - Do not request labeler code just to register a new drug establishment

# Registering Drug Establishments in SPL Format

# Registering Drug Establishments in SPL Format

- Each Registrant (owner/operator firm) must submit **one** SPL file with registration information for all of its facilities (unlimited amount of domestic or foreign establishments permitted per file)
- Subsidiaries can be considered as registrants in ER SPL files
- **Enter current registration year in effective date field**



# Establishment Registration SPL Document

Product Information	
Product Type	ESTABLISHMENT REGISTRATION

Registrant - Acme, Inc. (2223334441)			
Contact	Address	Telephone Number	Email Address
Deborah Tyler	Address: 222 Bonifant Avenue City, State, Zip: Fort Washington, PA, 35295 Country: USA	+1-800-435-4585	deborah.tyler@acme.com

Establishment			
Name	Address	ID/FEI	Operations
Acme Manufacturing, Inc.	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	475859252	manufacture
Contact	Address	Telephone Number	Email Address
Pam Jamison	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	+1-800-778-8359	pam.jamison@acme.com

# Establishment Registration

## SPL Document cont...

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Establishment			
Name	Address	ID/FEI	Operations
Acme International	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	98583572	manufacture, analysis
Contact	Address	Telephone Number	Email Address
Etienne St. Champs	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	+33-538-5859	etienne.st-champs@acme.com
US Agent (ID)	Address	Telephone Number	Email Address
Acme USA (359582424)		+1-800-999-5542	jacob.goodman@acme.com
Importer (ID)	Address	Telephone Number	Email Address
Franklin Imports (252597793)		+1-888-444-5835	paula.johansen@franklin.com

Revised: 09/2008

# Registration Number

- “FDA intends to use the Data Universal Numbering System (D-U-N-S®) as the registration number for the electronic system. Therefore, to facilitate and expedite processing of the SPL file, the registrant should submit their D-U-N-S® Number with the registration information. If the business entity does not submit a D-U-N-S® Number with its submission, FDA intends to make arrangements for obtaining a D-U-N-S® Number for that entity. An explanation of the D-U-N-S® Number and how to obtain one is described in section IV.B of this document.”

\*\*\*from final “eList” guidance document.

# Types of Operations

- Acceptable types of operations for establishments:
  - ANALYSIS
  - LABEL
  - MEDICATED ANIMAL FEED MANUFACTURE
  - MANUFACTURE
  - PACK
  - PARTICLE SIZE REDUCTIONRECOVERY
  - RECOVERY
  - RELABEL
  - REPACK
  - STERILIZE
- **Unacceptable types of operations for establishments:**
  - IMPORT
  - UNITED STATES AGENT

\*\*\* More types of operation **terms** will be added in future

# US Agent

- **US Agent**
  - Name
  - DUNS number
  - Telephone Number
  - Email Address

# US Agent

- No more **paper** US Agent letters -  
Submission of information about US Agent  
replaces the paper letter
- Each foreign establishment in an ER SPL  
should have a US agent

# Importer

- *...under section 510(i)(1)(A) of the Act, the name of each importer that is known to the establishment (this means each U.S. company or individual in the United States that is an owner, consignee, or recipient, of the foreign establishment's drug, that is imported into the United States. An importer does not include the consumer or patient who ultimately purchases, receives, or is administered the drug, unless the foreign establishment ships the drug directly to the consumer or patient.); and the name of each person who imports or offers for import (this means the name of each agent, broker, or other entity, other than a carrier, that the foreign drug establishment uses to facilitate the import of their drug into the United States).*

*(from "Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing")*

# Importers

- **Importer (if applicable)**
  - Name
  - DUNS number
  - Telephone Number
  - Email Address
- May or may not be an importer for each foreign establishment – Foreign establishments which do not export a drug product that is not imported into the US does not need to include importer data elements.



# ER SPL Notes

- Include postal code for all establishments unless one does not exist.
- Entering provinces - The province, "BC", goes in the <state> tag.
- For now, add “-” to empty state and zip code field (for foreign drug establishment locations)
- No limit to amount of importers
- No limit to number of establishments in one SPL
- Use ISO-3166-1 Country Code
- Use “USA” as the country code for Puerto Rico

# Updating an ER SPL

- Update information for an **electronically** registered establishment
- Update **anytime** during year **or** for annual registration
  - Open the previous SPL file and fill in the new information **without changing the other existing information.**
  - Use
    - new id root
    - new version number
    - original setId root
    - appropriate effective time.

# Adding a New Establishment

- Add a new establishment to your ER SPL file:
  - Open the previous SPL file
  - Fill in the information on a new establishment **without changing the information on the other establishments.**
  - Use
    - **new** id root
    - **new** version number
    - **original** setId root
    - appropriate effective time.

# Removing an Establishment

- Remove a previously **electronically** registered establishment
  - Open the previous ER SPL file, **without changing the existing information on the other establishments**, and remove the specific establishment information.
  - Use
    - **new** id root
    - **new** version number
    - **original** setId of your ER SPL
    - appropriate effective time.

# Establishment Re-Registration

## No Changes

- Applicable for registrants who have **previously electronically registered** drug establishments at least once.
- Simple process for annually re-registering establishments which have no changes
- Submit No Change Notification SPL

# Establishment Re-Registration

## No Changes

- No changes to registration information
  - Each year when the information is updated, if there is no change:
    - Create an SPL file with the *document type* **No change notification** with a **new** id root and **new** version number with the **original** setId and the appropriate effective time.
    - Registrant and establishment information is **not** included with an SPL file with the *document type* **No change notification**.

# Establishment No Change Notification SPL

<b>Product Information</b>	
<b>Product Type</b>	NO CHANGE NOTIFICATION

Revised: 04/2008

# Going Out of Business?

- Applicable for registrants who have **previously electronically registered** drug establishments at least once.
- If the registrant goes out of business, create an SPL file with the *document type* **Out of business notification** using a **new** id root and **new** version number with the **original** setId and the appropriate effective time.
- Registrant and establishment information is not included with an SPL file with the *document type* **Out of business notification**.



# Establishment Out of Business Notification

<b>Product Information</b>	
<b>Product Type</b>	OUT OF BUSINESS NOTIFICATION

Revised: 09/2008

# Certified 2656 Paper Form?

- No certified paper forms for e-registered establishments
- Check DFARS website for electronically registered establishments
- FDA inspectors requesting paper 2656 form?
  - Recommend DFARS website
  - If necessary, contact your local District Office as part of the conflict prevention and resolution process.

# Listing/Content of Labeling SPL

# Content of Labeling/Listing File

- One file contains:
  - Content of labeling (drug facts, package insert)
  - Images (jpeg only) of carton/container image(s)
  - Data about the establishments and labeler and, if necessary, registrant)
  - Product Data Elements

# eLabeling Repository

- Beginning June 1, 2009, the eList system is the key repository for labeling (including post-approval labeling submitted to comply w/Electronic Labeling Rule.
- Eliminate duplicative labeling submissions

# Listing by PLD

- “If a drug product is listed by the PLD, it should not also be listed by the owner(s) of the registered establishment(s) that manufactured, prepared, propagated, compounded or processed (which includes, among other things, repackaging and relabeling) the listed drug(s).”

\*\*\*from final “eList” guidance document

# UNII Update

- Substance Registration System team is assigning UNIs as quickly as possible
- UNIs – Request missing UNIs via e-mail to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov)
- Need to eList right away?
  - If UNIs for inactive ingredients are missing, request UNII, but leave out names of inactive ingredients in product data elements section until UNIs are assigned. Include in next elisting update

# Data Relationships



# e-Files for Drug Establishment Registration & Listing – SPL Format

- NDC Labeler Code Request
- Establishment Registration
- Content of labeling (CoL)/Listing

# Order of Submissions

1. NDC Labeler Request (LCR) and Establishment Registration (ER) SPL
  2. CoL/Listing SPL
- CoL/Listing validates against data submitted in NDC LCR and ER SPL

# SPL Errors

# Correcting an SPL with Validation Error

- Correct SPL file validation error
    - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.
- \*\*\*SPL file **never** made it into the FDA eList system\*\*\*

# Correcting Mistakes in Valid SPL Just Submitted

- Correct a mistake in an SPL file just submitted
    - Open the SPL file, correct the mistake,
    - Use
      - **new id root**
      - **new version number**
      - **original setId root**
      - appropriate effective time.
- \*\*\*SPL file was **valid** and loaded into FDA eList system

# Error Messages cont...

- Contact FDA at [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov) regarding questions or comments regarding error messages

# Sample System Generated Validation Report

**Validation Report**

Document b57873cf-1ad4-4f30-bdb6-4f99baf5e46b (version 1) validated on 200-05-20 at 14:35 contained 2 errors.

**Overview of Errors**

1. [Value of version number must be greater than the value of any previously submitted version for the same setId](#)
2. [id must be unique across all documents](#)

**XML View**

Click on the XML tag to expand or collapse. The marks identified like this **2** indicate thus many errors are in the collapsed element. Errors are shown in **red comments, such as this**. Double-click to expand all.

```
<document xsi:schemaLocation="urn:hl7-org:v3 http://www.accessdata.fda.gov/spl/schema/spl.xsd" v:schemaVersion="2.0">
  <!-- Value of version number must be greater than the value of any previously submitted version for the same setId [1.3.16, go back] -->
  <id root="b57873cf-1ad4-4f30-bdb6-4f99baf5e46b">
    <!-- id must be unique across all documents [1.3.5, go back] -->
    </id>
    <code code="51726-8" codeSystem="2.16.840.1.113883.6.1" displayName="NDC LABELER CODE REQUEST"/>
    <effectiveTime value="20090520"/>
    <setId root="a41f2c3e-3b09-49d4-8aaf-3537ce86b757"/>
    <versionNumber value="1"/>
    <author ... >
    <component ... >
  </document>
```

# Common Errors

- Uploading only XML file (Upload folder containing SPL (XML) file)
- Spaces preceding or following e-mail or telephone number
- Zipping files
- Sending listing or registration file to Gateway “center” other than “OC”
- Mismatched DUNS Numbers



# Test Your SPL R4 Docs

- Provision of SPL R4 Validator Tool
- Test SPL R4 files prior to submission
- Discover ~**95%** of validation errors prior to submission.
- Schematron technology – permits quick updates to validation procedures
- FDA in collaboration with Pragmatic Data makes available a validation tool:  
[Pragmatic Validator Lite™](#)

# NEW FDA Website

- New link to FDA Data Standards Council website -  
<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>
- Updated link which is different than link in final guidance document.

# Q&A

## Questions

**THANK YOU  
FOR  
YOUR  
ATTENDANCE**